Atomic Bomb Studies at ABCC/RERF Overview

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Early Years

- A-bomb explosions in August 1945
  - Acute deaths (through December 1945)
    - Hiroshima: 90,000-120,000 of 330,000
    - Nagasaki: 60,000-80,000 of 250,000
- US Government established Atomic Bomb Casualty Commission (ABCC) to study late effects, 1947
  - A genetic study of 80,000 newborn infants, 1948-
  - Leukemia registry, late 1940s

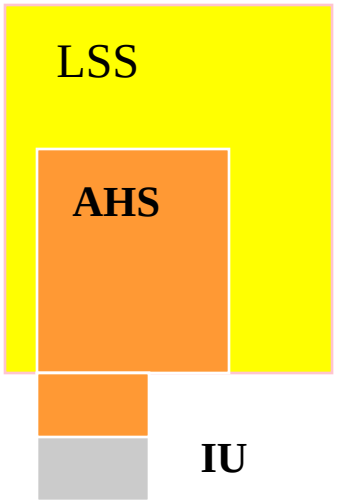
Francis Committee, 1955

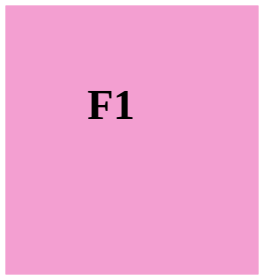
- Thomas Francis, Jr
- Seymour Jablon
- Felix E. Moore

- ..one of the mutagenic effects might ..increase congenital malformations, but little is known about possible somatic effects.
- ..emphasizes the critical importance of continuity. An important element.. is the establishment of fixed, well-defined groups of exposed and non-exposed person ("Unified study design")
  - Establishment of "cohort" populations and long-term follow-up mechanisms
  - Field study to collect information (location, shielding, acute effects) for exposure assessment

Cohorts

Cohort	Size
Life Span Study (LSS)	120,000
Adult Health Study (AHS)subset	*22,000*
In-utero exposure (IU)	3,300
Adult Health Study subset	*1,100*
F_1 generation	80,000





LSS Cohort

- Survivors within 2.5 km of the bombings
  - Lived in Hiroshima and Nagasaki in 1950
  - Met certain conditions favorable for follow-up
  - Roughly half of all survivors <2.5 km
- Age/sex matched survivors within 2.5 -10 km
- Not-in-city (NIC)
  - Hiroshima/Nagasaki residents who were not in either city at the time of the bomb (ATB)

Follow-up Methods (1)

- Mortality
  - Since 1950
  - Virtually complete ascertainment regardless of residence through family registration system (*koseki*) and death certification
- Cancer incidence
  - Since 1958
  - Through Hiroshima and Nagasaki tumor registries

Follow-up (2)

- Pathology program
  - Autopsies in 1950s, 60s and 70s
  - Surgical pathology program
- Adult Health Study clinical follow-up
  - Subset of 22,000 persons in the contact area
  - Biennial health examination since 1957
  - Continued high participation, 70%
- LSS mail surveys
  - Roughly every 10 years since 1970
  - Lifestyle and risk factors

Strengths and Limitations of LSS

- Strengths
  - Large naturally-living population exposed at a wide rage of ages
  - Continuous follow-up of > 50 years
  - Comprehensive coverage of endpoints
  - Well-defined individual dose estimates
- Limitations
  - Can address only single exposure
  - Missing first 5 years

Principal Findings To Date

- Early excess of leukemia risk with a peak 5-10 years after exposure
- Gradual increase in solid cancer risk persisting for many decades – possibly throughout life
- Emerging evidence of excess non-cancer disease risk – notably of cardiovascular disease
- Age/time dependence of leukemia and cancer risks and dose response data – important for risk estimation

Solid Cancers

LSS Cohort by Dose

Colon dose (Sv)	Persons	Percent
<0.005	35,483	30%
0.005-	26,299	22%
0.05-	6,377	5%
0.1-	5,738	5%
0.2-	6,253	5%
0.5-	3,196	3%
1.0-	1,607	1%
2.0+	679	0.5%
Unknown	7,109	6%
Total survivors	93,741	78%
Not in city	26,580	22%
LSS total	120,321	100%

Although the dose response is largely driven by data at >1 Sv, substantial information can also be obtained on low dose risk.

LSS Solid Cancer Mortality 1950-1997

Dose, Sv	Subjects	Observed	Expected	Excess
< 0.005	37,458	3,833	3,844	0
0.005 -	31,650	3,277	3,221	44
0.1 -	5,732	668	622	39
0.2 -	6,332	763	678	97
0.5 -	3,299	438	335	109
1 -	1,613	274	157	103
> 2	488	82	38	48
Total	86572	9,335	8,895	440

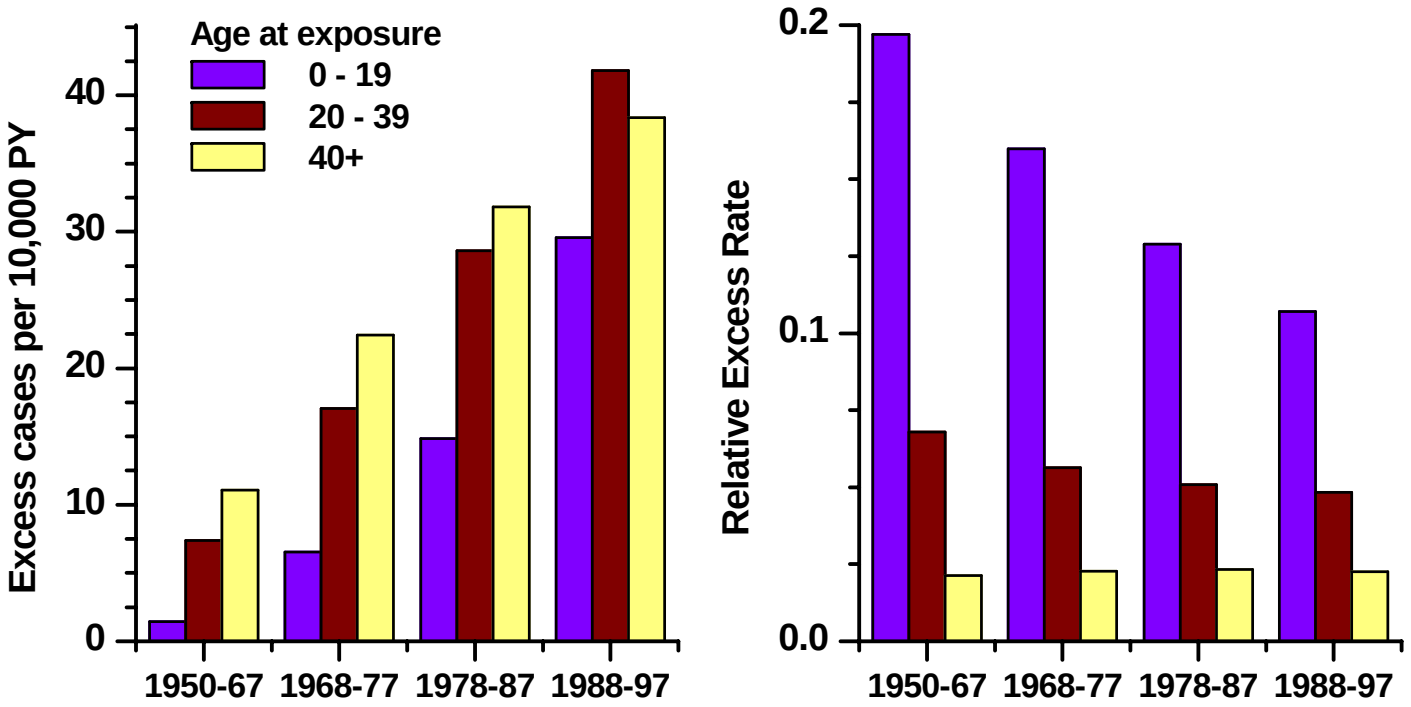
(LSS Report 13, Preston et al, 2003)

Solid Cancer
Temporal Patterns

Age at exposure	1950 - 67 Obs	1950 - 67 Excess No (Rate)	1968 - 77 Obs	1968 - 77 Excess No (Rate)	1978 - 87 Obs	1978 - 87 Excess No (Rate)	1988 - 97 Obs	1988 - 97 Excess No (Rate)
<20		9 *(1.5)*	189	22 *(6.5)*	434	49 *(14.9)*	954	93 *(30.0)*
20 -	457	28 *(7.4)*	632	35 *(17.0)*	1,055	51 *(28.6)*	1,219	57 *(41.8)*
>40	2,055	42 *(11.1)*	1,192	27 *(22.5)*	769	19 *(31.8)*	334	6 *(38.4)*
Total	2,557	79	2,013	84	2,258	119	2,507	156

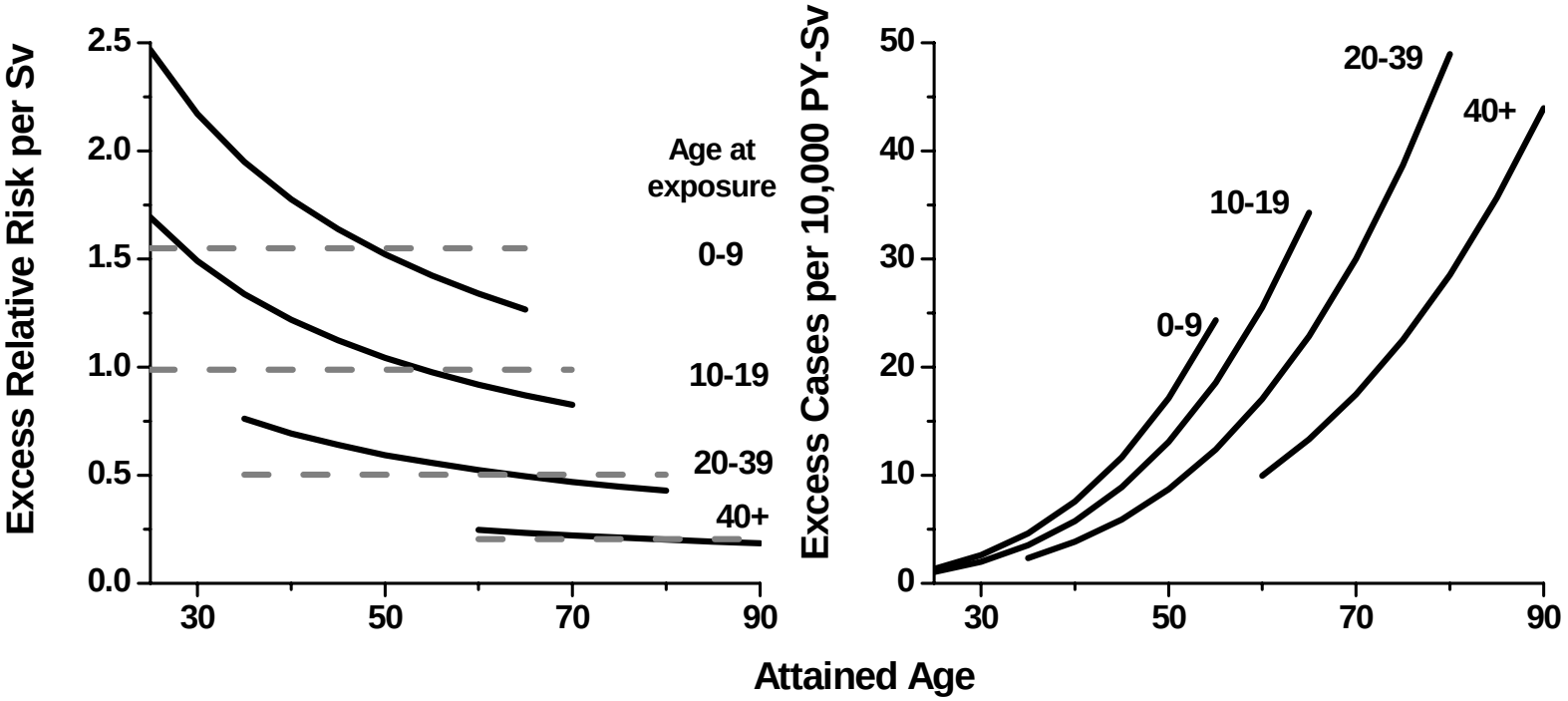
(LSS Report 13, Preston et al, 2003)

Solid Cancer:
Absolute and Relative Excess Rates



(LSS Report 13, Preston et al, 2003)

Solid Cancer:
ERR and EAR by Age



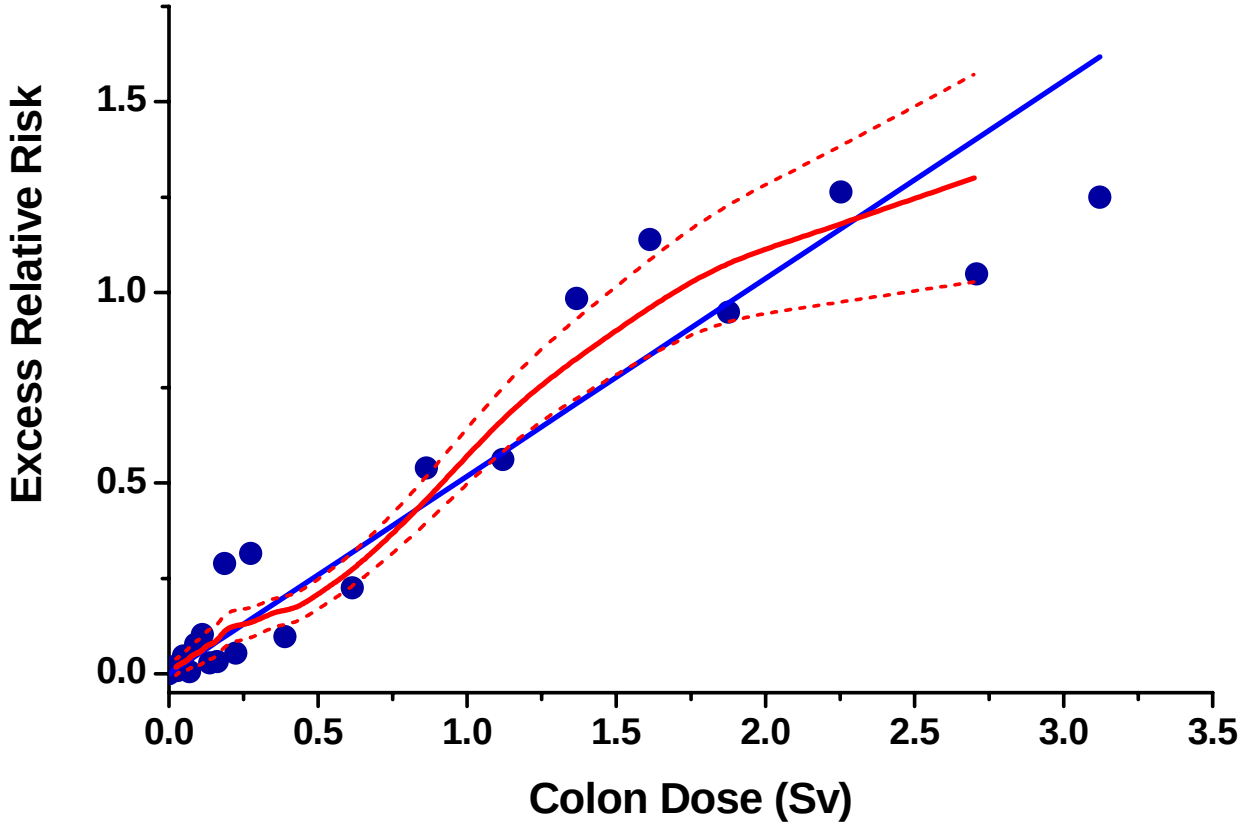
(LSS Report 13, Preston et al, 2003)

Age at Exposure and Vital Status

Age at exposure	People in 1950	Alive in 1998
0 - 9	17,824	16,243 (91%)
10 - 19	17,558	14,030 (80%)
20 - 29	10,883	7,158 (66%)
30 - 39	12,266	3,810 (31%)
40 - 49	13,491	549 (4%)
> 50	14,550	11 (0%)
Total	86,572	41,801 (48%)

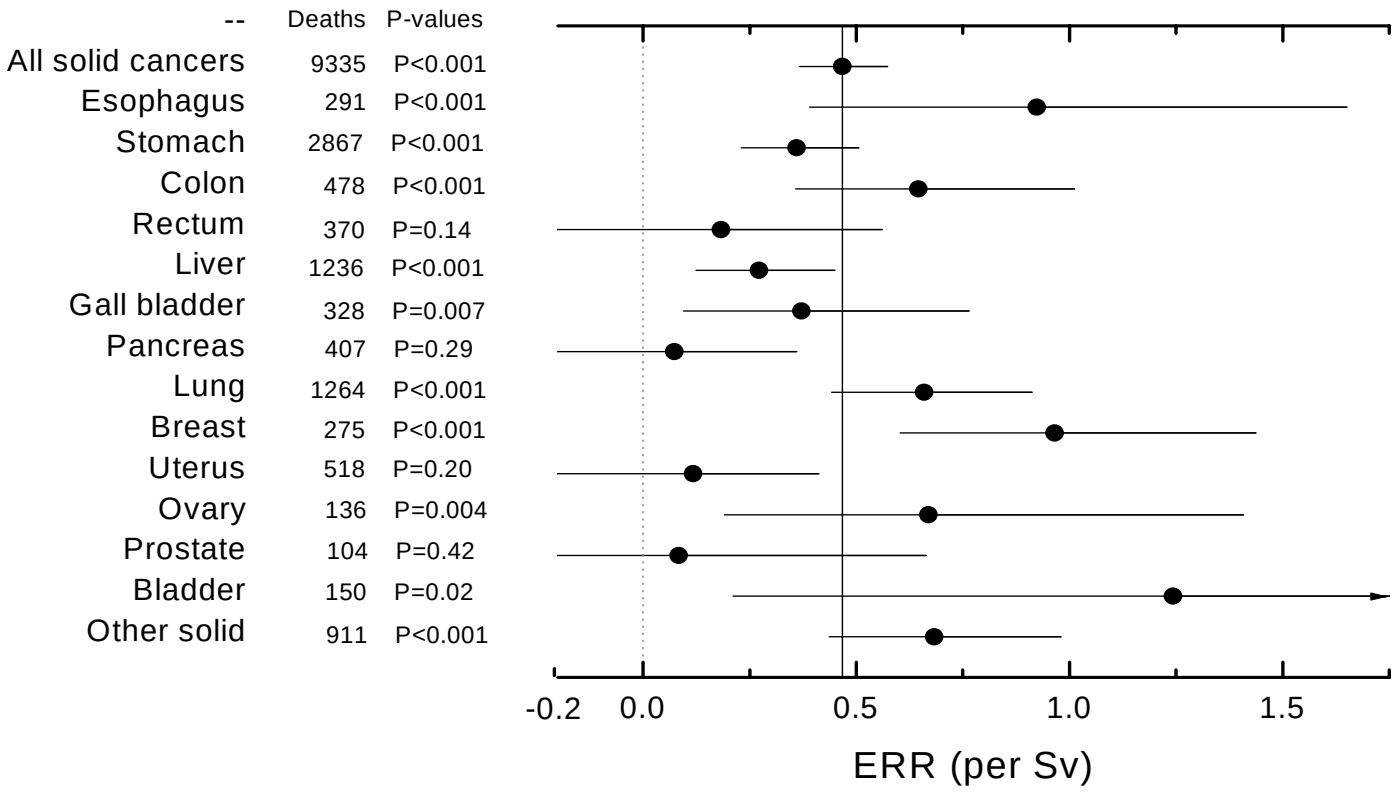
(LSS Report 13, Preston et al, 2003)

Solid Cancer Dose Response



(LSS Report 13, Preston et al, 2003)

Site-specific ERRs



(LSS Report 13, Preston et al, 2003)

Leukemia

Leukemia mortality

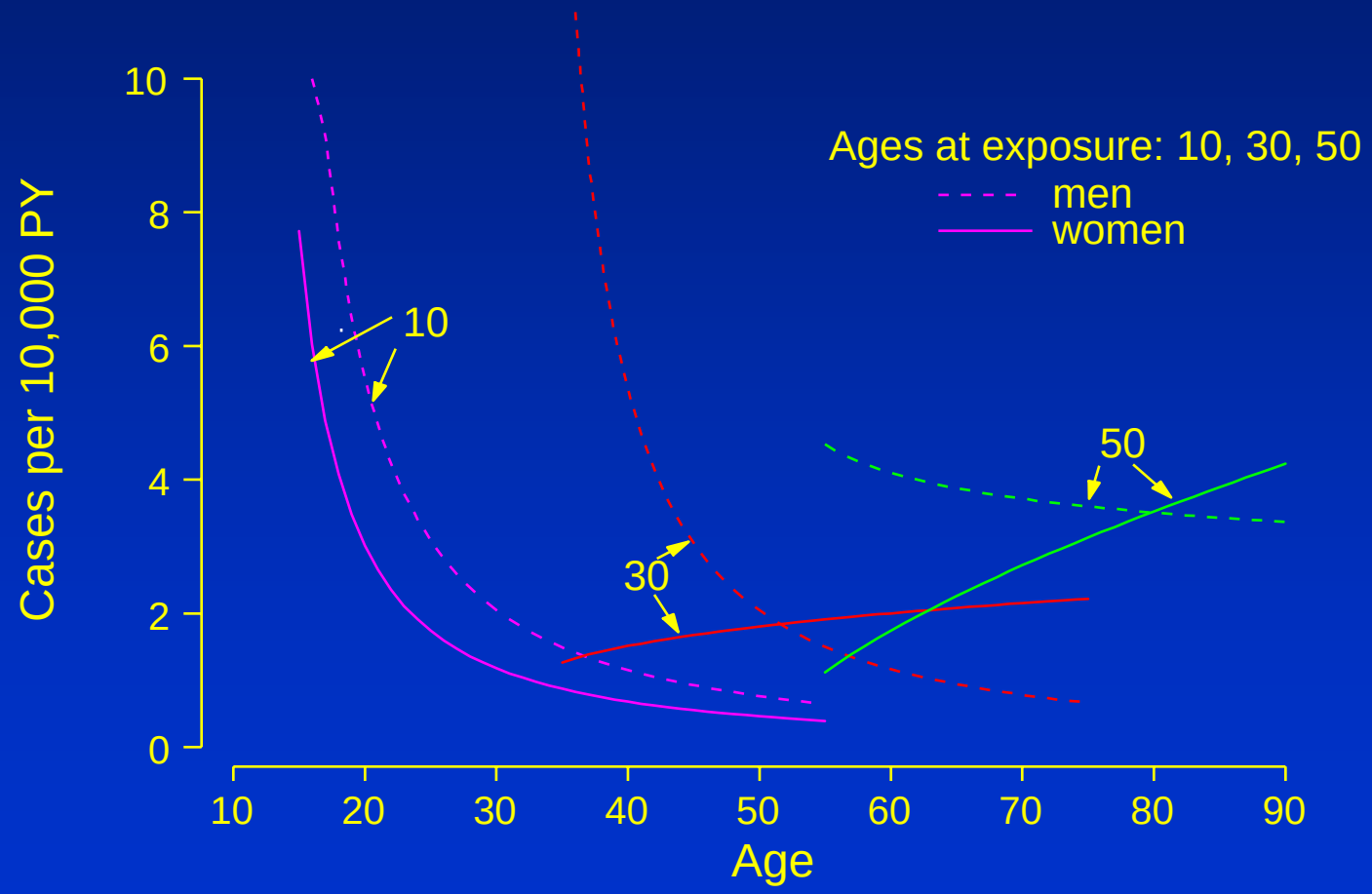
1950 - 1990

Dose (Sv)	Subjects	Obs.	Exp.	Excess
< 0.005	35,458	73	65	8
0.005 -	32,915	59	63	-4
0.1 -	5,613	11	12	-1
0.2 -	6,342	27	13	14
0.5 -	3,425	23	7	16
1 -	1,914	26	4	22
> 2	905	30	2	28
Total	86,572	249	166	83

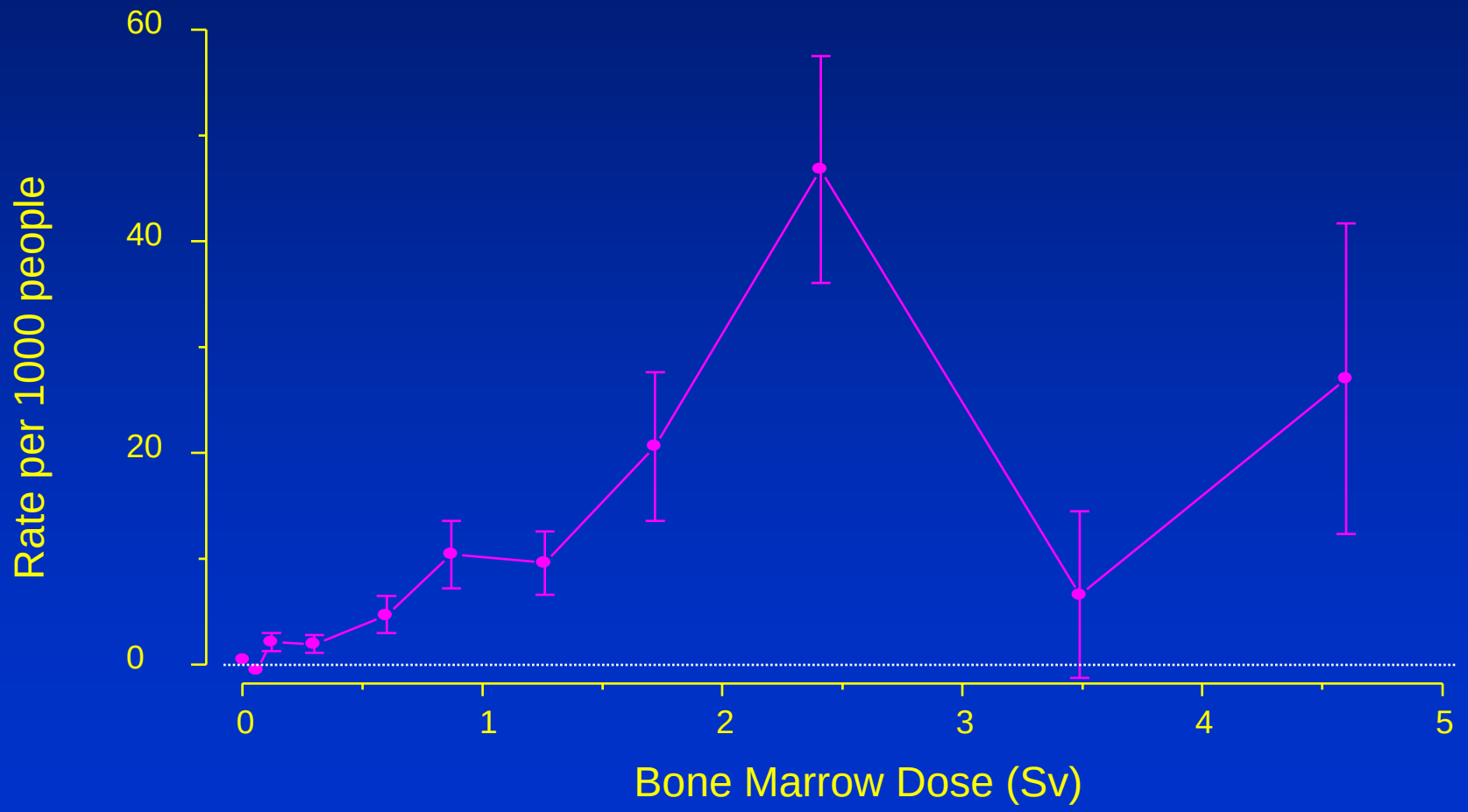
Leukemia
Temporal Patterns

Age at exposure	1950 - 75		1976 - 85		1986 - 90	
	Obs.	Excess	Obs.	Excess	Obs.	Excess
0 - 9	29	20	3	-3	3	-2
10 - 19	29	18	7	-2	7	1
20 - 29	21	12	8	1	3	-1
30 - 39	21	6	22	12	7	2
40 - 49	37	15	15	4	7	3
50+	23	-1	6	2	1	0
Total	160	70	61	14	28	3

Leukemia Excess Absolute Risk



Leukemia Dose Response



Non-cancer Diseases

Non-cancer Mortality 1950-97

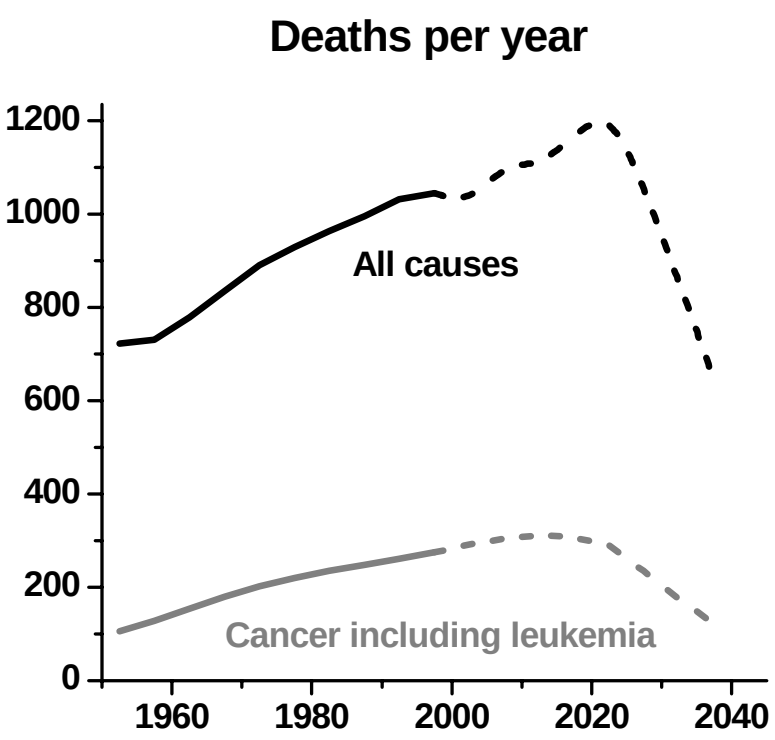
Dose, Sv	Obs	Expected	Excess
<0.005	13,832	13,954	0
0.005-0.1	11,633	11,442	17
0.1-0.2	2,163	2,235	17
0.2-0.5	2,423	2,347	47
0.5-1	1,161	1,075	61
1-2	506	467	68
2+	163	111	40
Total	31,881	31,631	250

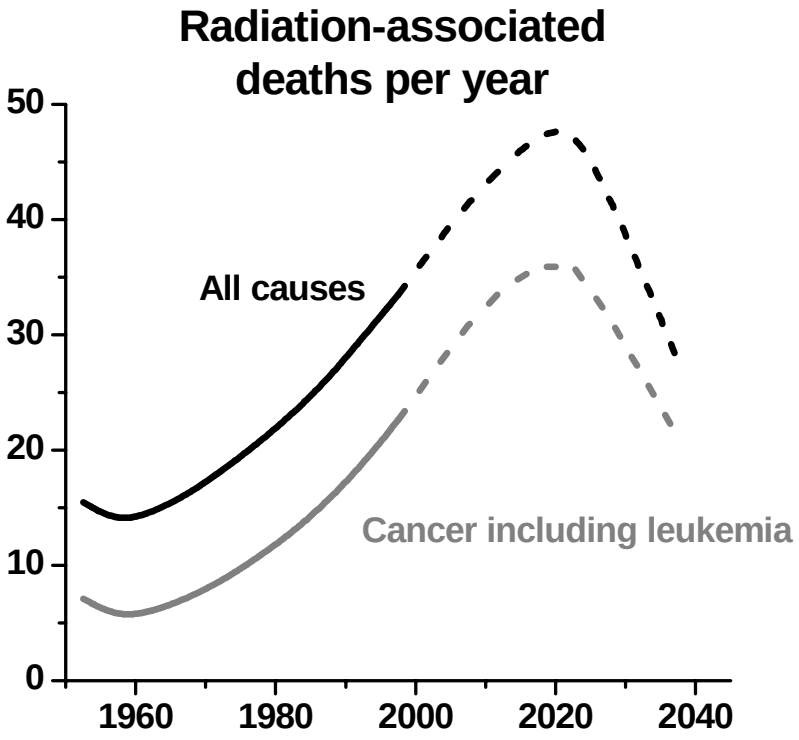
(LSS Report 13, Preston et al, 2003)

Magnitude of Risk

	1950-1997		1991-1997	
	Deaths	Excess	Deaths	Excess
Cancer	9,335	440	1,756	114
Non-cancer	31,881	250	4,760	66

Future





(LSS Report 13, Preston et al, 2003)

In-utero Cohort

- Cohort of 3,300 persons
- Exposure throughout all gestational period
- DS86 maternal uterine dose
  - 800 persons >0.01 Sv
- Mostly followed since birth
- 96% alive

In-utero Findings

- Severe mental retardation, brain damage
- Absence of childhood leukemia
- Increased solid cancer risk
  - Cancer mortality risk: in-utero vs early childhood exposure (Delongchamp et al, 1997)

Cancer Mortality
Ages 17-46

	PY/10^4	Leukemia		Solid cancer	
		Cases	Rate	Cases	Rate
Exposed; in-utero	**4.1**	**2**	**0.5**	**8**	**2.0**
Exposed: childhood	**23.0**	**24**	**1.0**	**56**	**2.4**
Controls	**39.5**	**4**	**0.1**	**57**	**1.4**

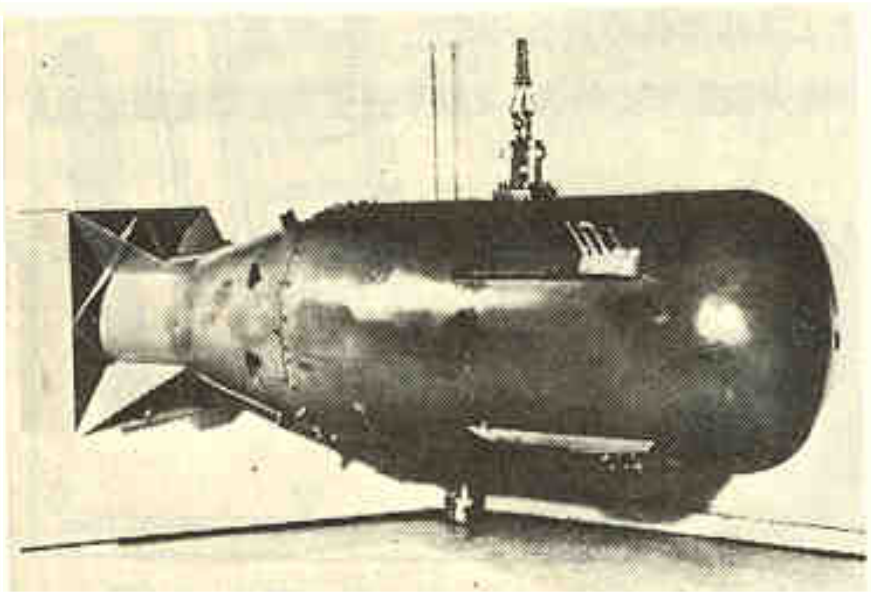
Solid Cancers

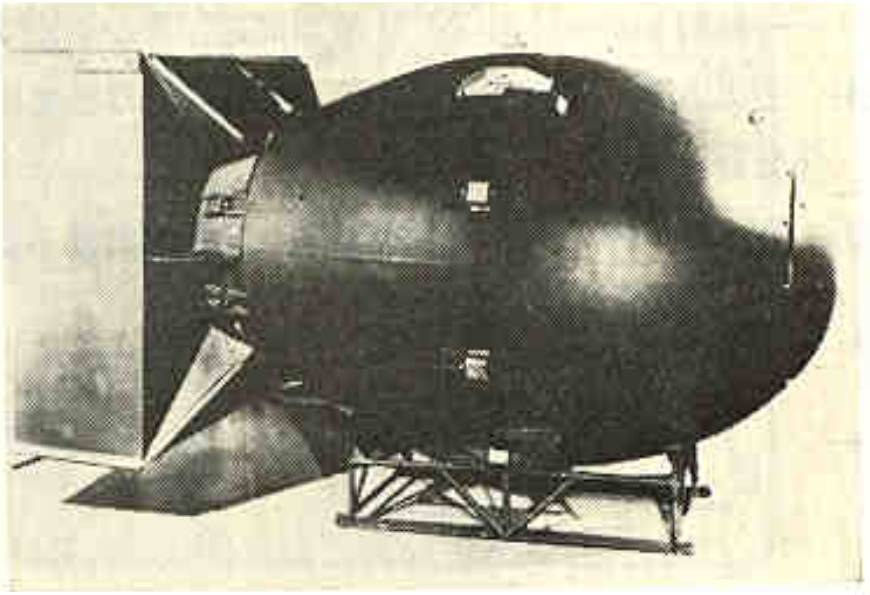
Ages 17 - 46

Exposed	Deaths	ERR/Sv
In utero	8	2.4 (0.3, 6.7)
Ages 0-5	56	1.4 (0.4, 3.1)

A-Bomb Dosimetry

Bombs

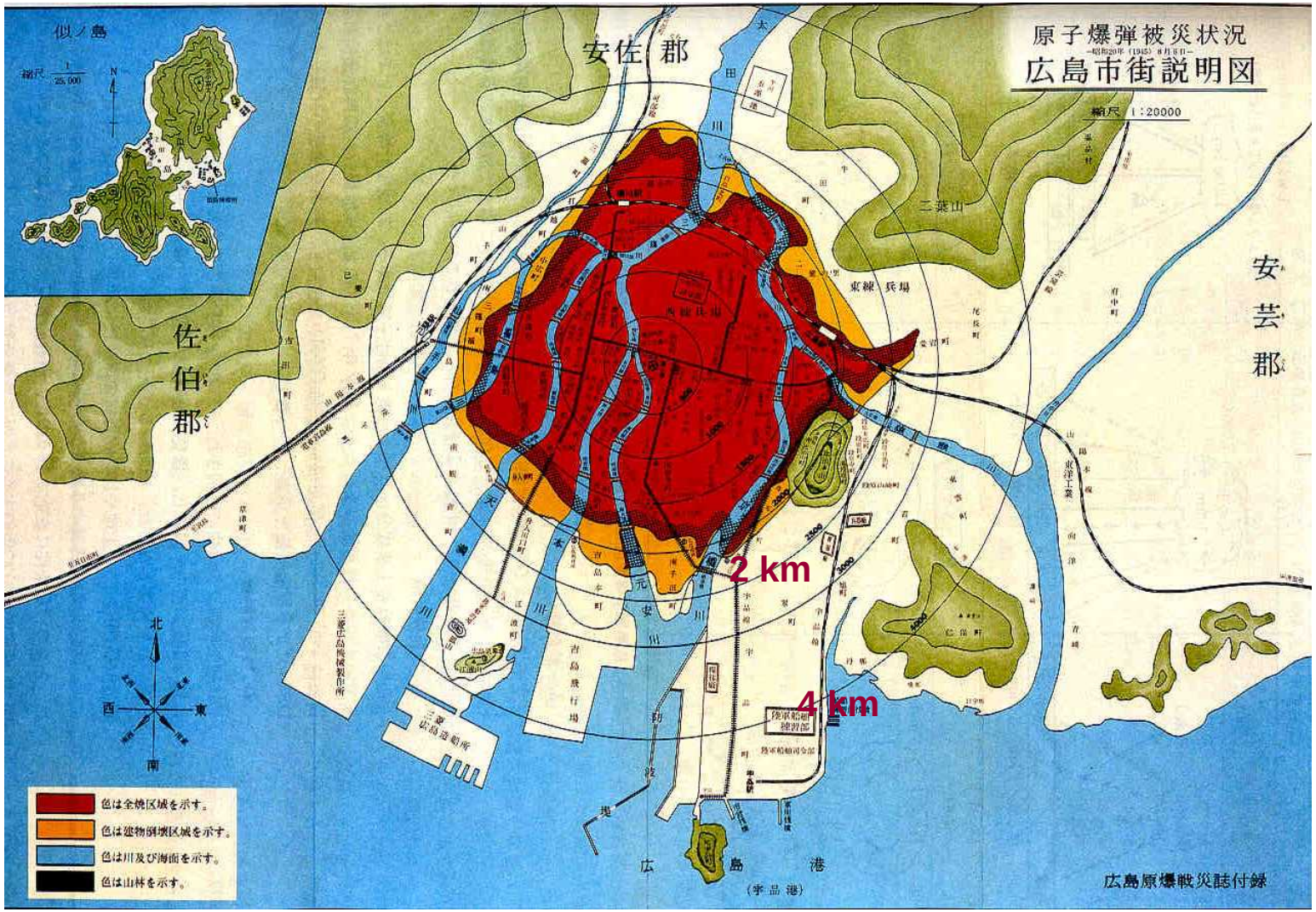




Hiroshima
^{235}U bomb, TNT 12.5 kt
“Little Boy”

Nagasaki
^{239}Pu bomb, TNT 22kt
“Fat Man”

HIROSHIMA



Completely burned from fire

Structural damage

Dosimetry System 86 (DS86)

Provides individual dose estimates (gamma and neutron doses for 15 organs) based on:

- Survivor's location ATB
- Shielding situation ATB
- Models
  - For radiation released, transportation through air, passage through physical structure and human tissue
  - Validated by measurements of exposed materials

FIGURE 1.5 Photograph made in 1958 during a weapons test at the Nevada Test Site. The Japanese house replicas are in the foreground, and the collimators used to measure the angular distributions of the neutrons and gamma-ray fields are in the background.

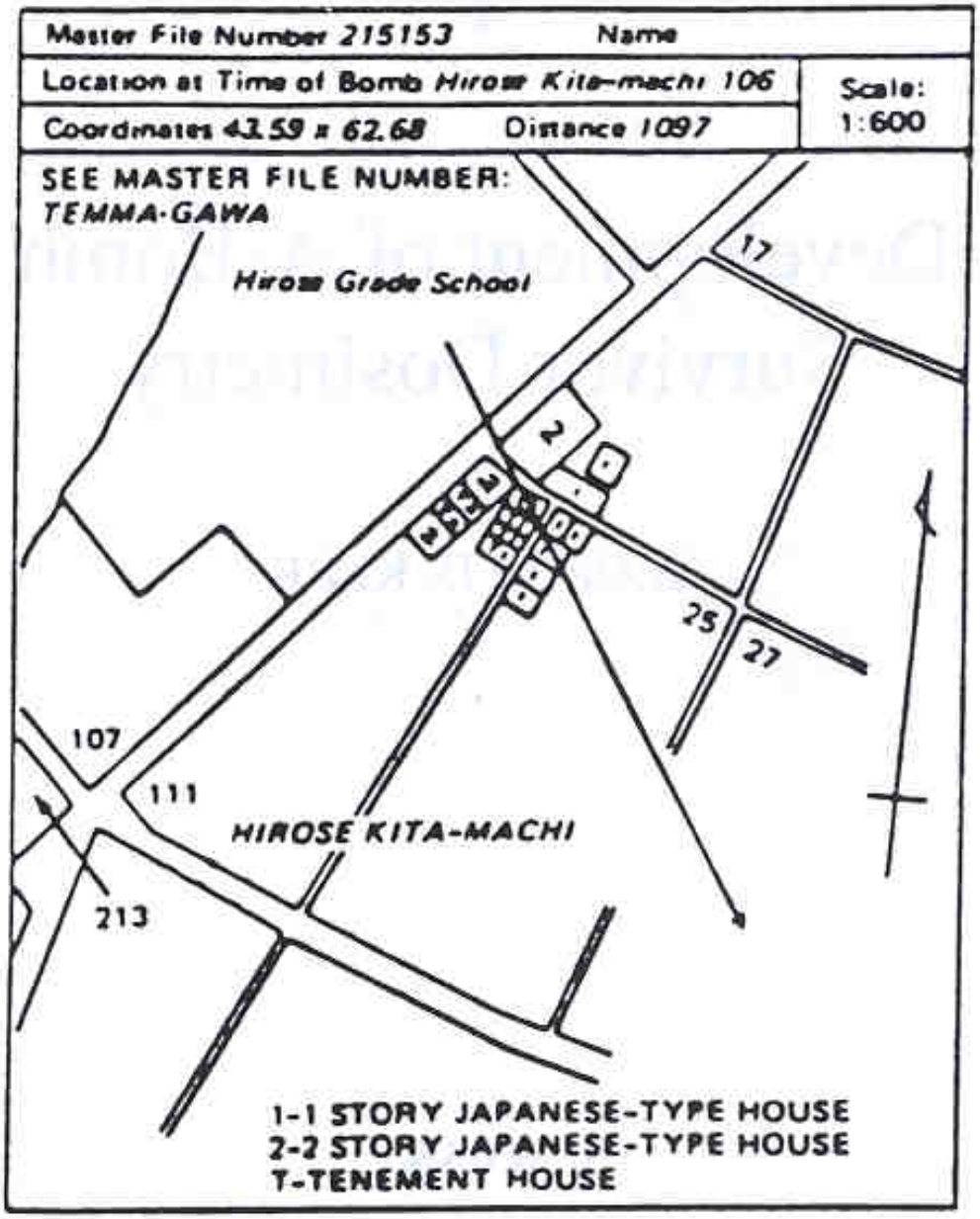


FIGURE 1.1(a) Example of a shielding history for a survivor exposed inside a one-story Japanese-type house in Hiroshima.

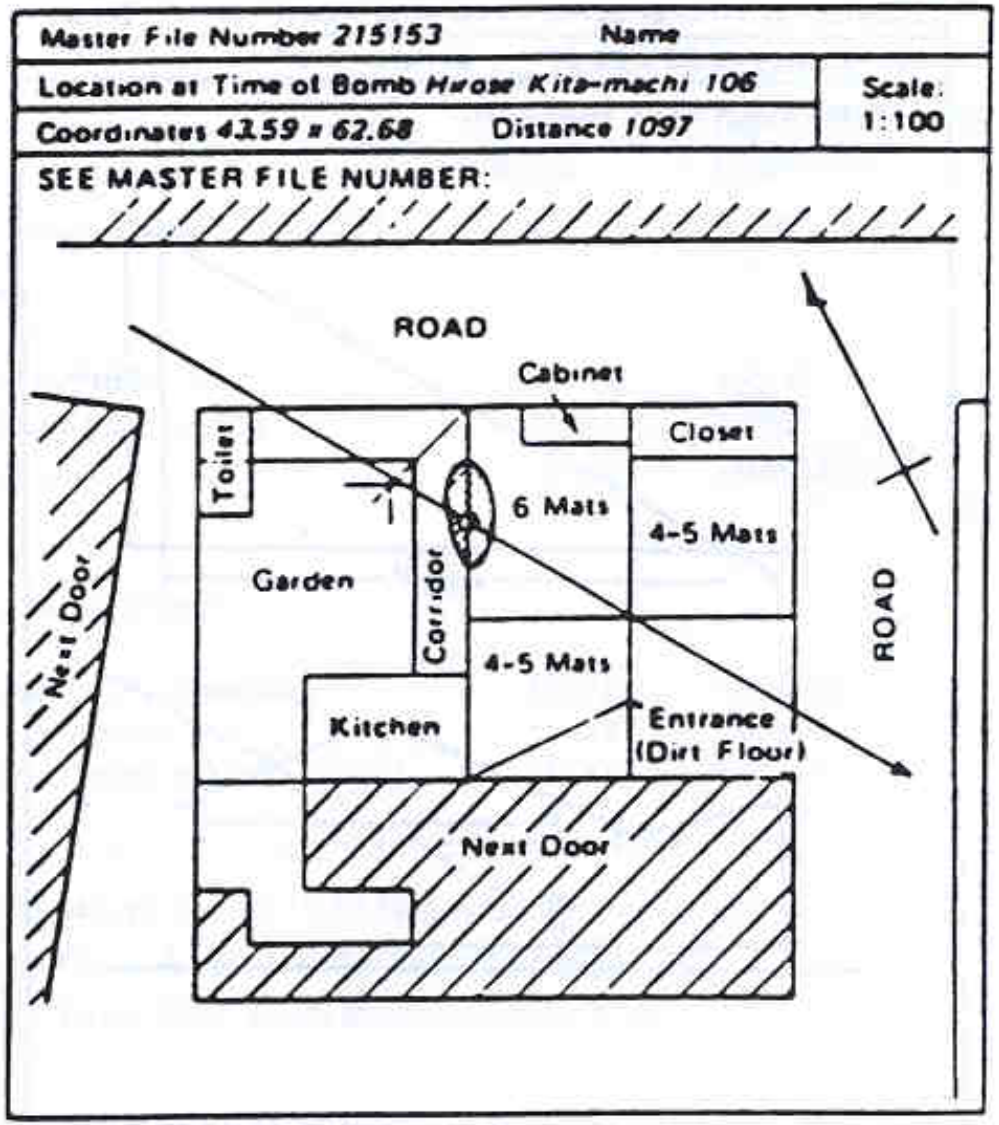


FIGURE 1.1(b) Example of a shielding history for a survivor exposed inside a one-story Japanese-type house in Hiroshima.

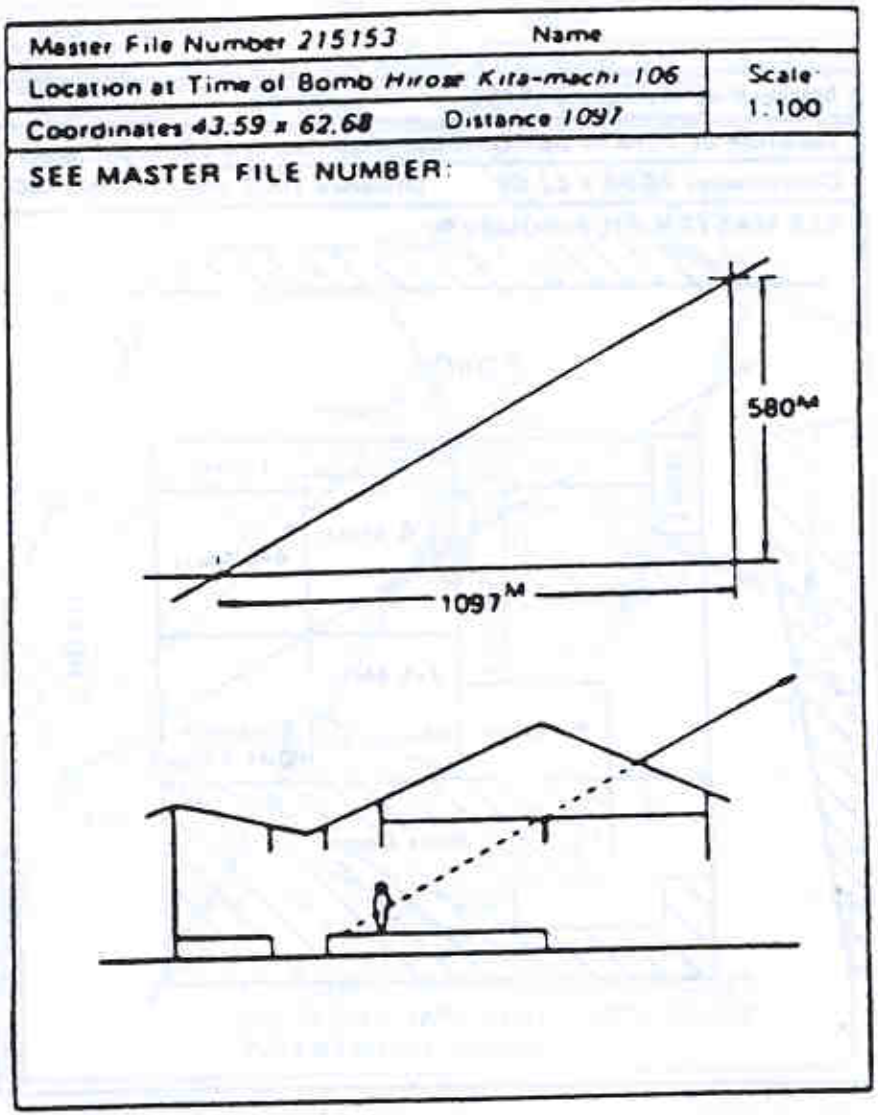


FIGURE 1.1(c) Example of a shielding history for a survivor exposed inside a one-story Japanese-type house in Hiroshima.

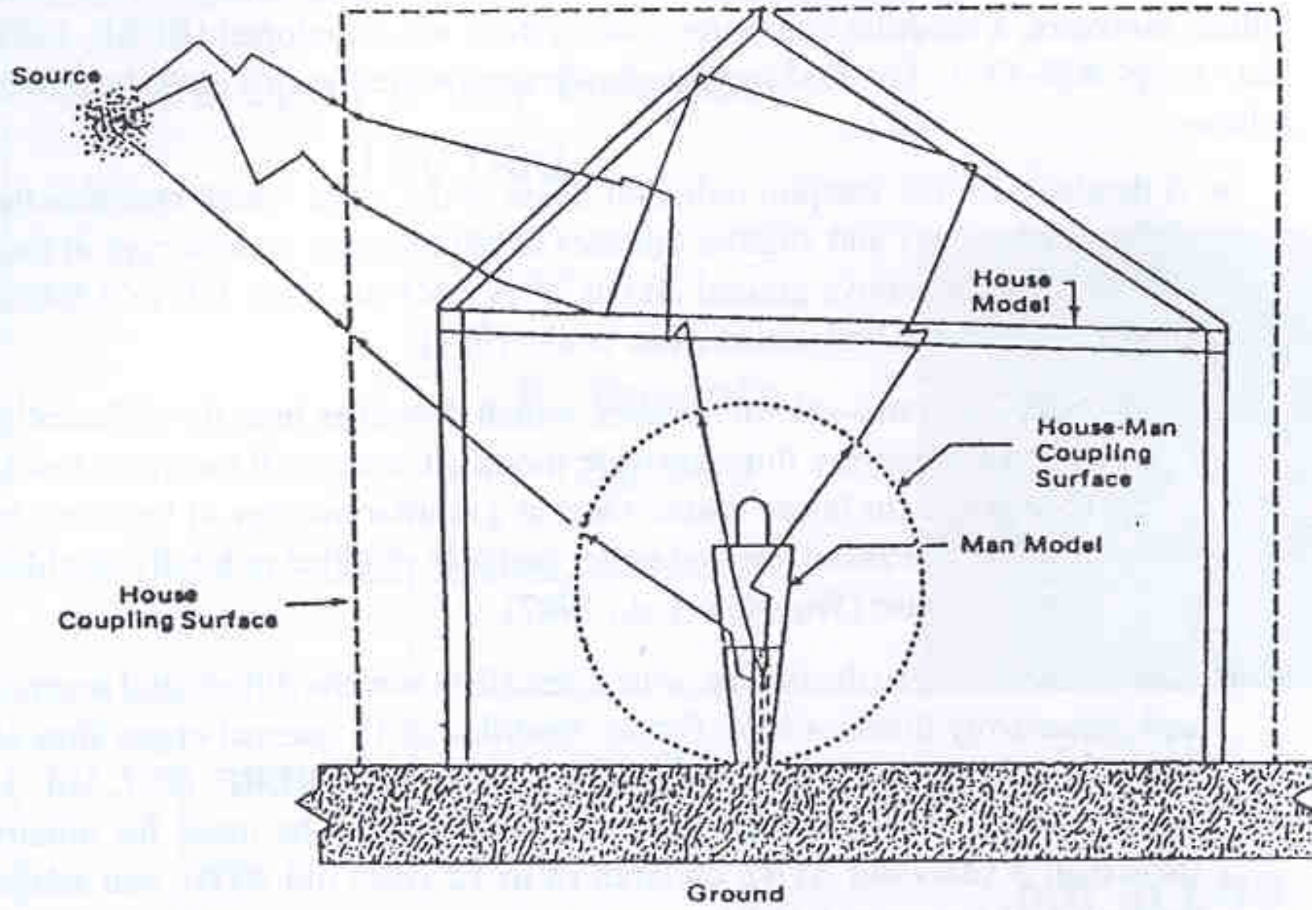
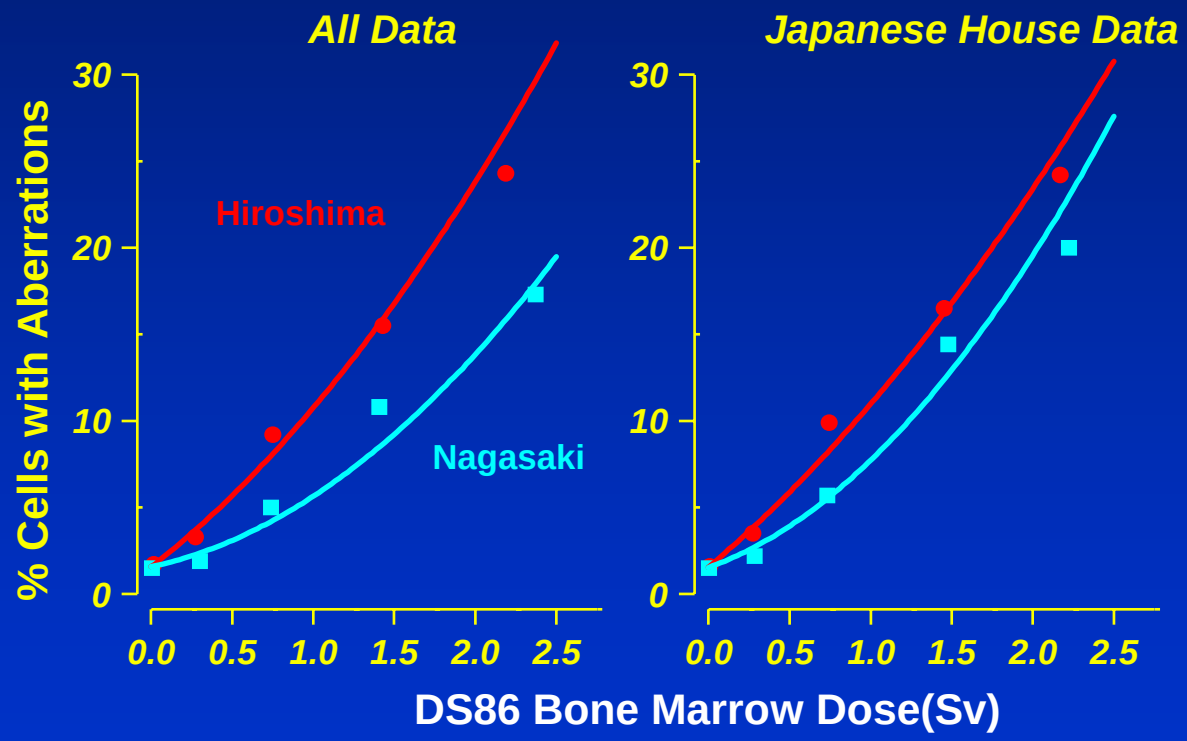


FIGURE 1.8 Illustration of the overall DS86 coupling procedure for dose estimation for individual A-bomb survivors with shielding histories.

Chromosome aberration vs DS86



DS02 Preliminaries

- DS02 is replacing DS86
- Small changes in dose estimates
  - Gamma doses increased slightly
  - Neutron doses decreased at ranges of interest
- Slight decreases in cancer risk estimates
  - ~7% decrease for solid cancer
  - ~15% decrease for leukemia
- Virtually no impact on shape, gender or age-time patterns